

REMARKS

Prior to the present submission, claims 1-17, 37, and 38 were pending in the application. Claims 18-36 were canceled by prior amendment.

Claims 2, 4, 6, 10, 12, 14, 16, 37, and 38 are canceled herein without prejudice or disclaimer. Applicants reserve the right to pursue these claims, or claims having the subject matter of canceled claims, in this or other related applications.

Claims 1, 3, 8, 11, and 17 are amended herein. The amendments are made in an effort to clarify the subject matter of the claims for the benefit of the Examiner to advance prosecution, and to make the subject matter and antecedent basis for recited claim elements of dependent claims consistent with the claims from which they depend.

Claim 1 has been amended solely to advance prosecution and more clearly set forth particular embodiments of the invention. Support for the amendments to claim 1 can be found throughout the specification, for example, at least on page 7, paragraph [0022], page 9, paragraph [0028], page 33, paragraph [0116] of the application as filed, as well as Examples 3 and 5, including the Tables within the Examples (pages 104-106).

Claims 3, 8, and 11 have been amended only to conform to the subject matter of independent claim 1. Claim 17 has been amended to include the comparison of the assayed amount of BNP to a predetermined threshold level. Support for this amendment can be found, for example, at least in Example 3 and paragraphs [0022] and [0023] on page 7 of the specification as filed.

New claims 39-46 have been added. New claims 39 and 40 find support, for example, in paragraph [0023] on page 7 of the specification as filed and Example 3. New claim 41 finds support on page 33, paragraph [0116] of the application as filed. New claim 42 finds support at least on pages 39-45 “Exemplary Markers Related to Myocardial Injury”, paragraphs [0133]-[0141] of the specification as filed. New claim 43 finds support at least in claim 11 as filed and

the specification pages 45-56 (paragraphs [0141]- [0152]). Claims 44 and 45 find support in the specification on page 107, paragraph [0122] and in Example 3 of the application as filed, for example in paragraphs [0085], [0097], and [0255], and the tables of Example 3 on pages 104-106. Support for new claim 46 finds support in paragraphs [0116] and [0122] of the application as filed.

No new matter is introduced by the newly added claims and claim amendments.

Applicants respectfully request their entry. Upon entry of the amendments, claims 1, 3, 5, 7-9, 11, 13, 15, 17, and 39-46 will be pending in the application.

Reconsideration of the claims is requested in view of the foregoing amendments and the following remarks.

Claim Objection

Applicants have canceled claim 38, rendering the objection based on an error in claim dependency moot.

Rejection of claim 38 under 35 USC § 112, second paragraph

Applicants have canceled claim 38, rendering the rejection based on an error in claim dependency moot.

Rejection of claims 1-10, 13, and 15-17 under 35 USC § 112, first paragraph,

Written Description

Claims 1-10, 13, and 15-17 have been rejected as allegedly failing to meet the Written Description requirement of 35 USC § 112, first paragraph. Solely to advance prosecution, and not in acquiescence to the rejection, Applicants have amended claim 1 to incorporate the subject matter of claim 12. Claims 4 and 16 are canceled herein, Applicants assert that claim 1 as amended, and claims 3, 5, 7-9, 13, 15, and 17 that depend from claim 1 fully comply with the Written Description requirement of 35 USC § 112, first paragraph. Claims 2, 6, and 10 have

been canceled, rendering their rejection moot. Applicants therefore respectfully request that the rejection be reconsidered and withdrawn.

Rejection of claims 1-10, 13, and 15-17 under 35 USC § 112, first paragraph, Enablement

Claims 1-10, 13, and 15-17 have been rejected under 35 USC § 112, first paragraph as allegedly not supported by enabling disclosure in the specification. Solely to advance prosecution, and not in acquiescence to the rejection, Applicants have amended claim 1 to incorporate the subject matter of claim 12. Claims 4 and 16 are canceled herein, Applicants assert that claim 1 as amended, and claims 3, 5, 7-9, 13, 15, and 17 that depend from claim 1 fully comply with the Enablement requirement of 35 USC § 112, first paragraph. Claims 2, 6, and 10 have been canceled, rendering their rejection moot. Applicants therefore respectfully request that the rejection be reconsidered and withdrawn.

Rejection of claims 1-4, 9-12, 15, 16, 37, and 38 under 35 USC § 103(a)

Claims 1-4, 9-12, 15, 16, 37, and 38 have been rejected under 35 USC § 103(a) as allegedly obvious over Jackowski (U.S. Patent No. 5,710,008) in view of Buechler et al. (U.S. Patent No. 5,795,725), Baig (*American Heart Journal*, 1998, 135: S216-S230), Kline et al. (*Annals of Emergency Medicine*, Feb. 2000, 35: 168-180), and Zweig et al. (*Clinical Chemistry*, 1993, 39: 567-577). Applicants do not agree that claims 1-4, 9-12, 15, 16, 37, and 38 are obvious over the cited references. However, to advance prosecution, and not in acquiescence to the rejection, Applicants have amended claim 1 and canceled claims 2, 4, 10, 12, 16, 37, and 38. Applicants assert that claims 1, 3, 9, 11, and 15 are nonobvious with respect to the cited references for at least the following reasons.

When making a rejection based on obviousness, the Examiner must ascertain the differences between the claimed invention and the prior art. Section 2143.03 of the MPEP requires the consideration of every claim feature in an obviousness determination. To render claim 1 unpatentable, however, the Office must do more than merely consider each and every

feature for this claim. Rather, the asserted combination of the cited references must also teach or suggest *each and every claim feature*. See *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974) (emphasis added) (to establish *prima facie* obviousness of a claimed invention, all the claim features must be taught or suggested by the prior art). Indeed, as the Board of Patent Appeal and Interferences has recently confirmed, a proper obviousness determination requires that an Examiner make “a searching comparison of the claimed invention – *including all its limitations* – with the teaching of the prior art.” See *In re Wada and Murphy*, Appeal 2007-3733, citing *In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995) (emphasis in original). Applicants respectfully direct attention to MPEP § 2143, the instructions of which support the conclusion that obviousness requires at least a suggestion of all of the features of a claim, since the Supreme Court in *KSR Int'l v. Teleflex Inc.* stated that “there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006).

Because the cited references fail to teach or suggest all of the limitations of independent claim 1, the obviousness rejection under 35 U.S.C. § 103 cannot be sustained.

First, the references do not disclose a method of distinguishing among myocardial infarction, congestive heart failure, and pulmonary embolism as is recited in claim 1 as amended. Jackowitz et al. discloses a method for diagnosis of myocardial infarction (MI) or unstable angina (UA) as a cause of chest pain. Jackowitz does not disclose a method for distinguishing either of these conditions from pulmonary embolism (PE) or congestive heart failure (CHF), such that the alternative conditions can be positively diagnosed. Rather, Jackowitz discloses diagnosing each of MI or UA by the presence or absence of particular markers.

In contrast, the claimed method uses a set of marker proteins to distinguish between three conditions, in which when one or more of a cardiac troponin form, myoglobin, and creatine kinase-MB (CK-MB) is used to rule out myocardial infarction (MI), and an elevated level of D-dimer is detected, the subject can be characterized as having developed or of developing

congestive heart failure (CHF) or pulmonary embolism (PE), and CHF and PE can be distinguished from one another by the amount of BNP detected in the sample.

None of Jackowski, Buechler et al., Baig, Kline et al., and Zweig et al. teach or suggest a method that distinguishes between three conditions using a set of markers, in which the set of markers can provide characterize a risk of each of the three specific conditions. (Jackowski uses cardiac markers to rule out “noncardiac” causes of chest pain. This is not a condition, and none of the markers disclosed by Jackowski diagnose any specific noncardiac condition.) Moreover, nothing in the cited art teaches or suggests characterizing a subjects risk of developing or having developed MI, PE, or CHF based on a set of markers, in particular using the markers CK-MB, myoglobin, a cardiac troponin form, D-dimer, and BNP or a marker related to BNP to characterize a subject’s risk of developing or having developed MI, PE, or CHF.

Further, nothing in the cited art teaches the use of BNP as a marker to distinguish between two conditions, or in particular as a marker to distinguish between PE and CHF, in which D-dimer is found to be elevated in both conditions, as recited in claim 1 as amended.

Because obviousness requires at least a suggestion of all of the features in a claim (*In re Wada and Murphy*, citing *CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) and *In re Royka*, 490 F.2d 981, 985 (CCPA 1974)), and all of the features of claim 1 are not found in the cited references, claim 1 and claims 3, 9, 11, and 15 that depend from claim 1 are nonobvious under 35 USC § 103(a). Claims 2, 4, 10, 12, 16 have been canceled, rendering their rejection moot. In view of the foregoing, Applicants respectfully request that the rejection of claims 1, 3, 9, 11, and 15 be reconsidered and withdrawn.

Rejection of claims 5-8, 13, and 14 under 35 USC § 103(a)

Claims 5-8, 13, and 14 have been rejected under 35 USC § 103(a) as allegedly obvious over Jackowski (U.S. Patent No. 5,710,008) in view of Buechler et al. (U.S. Patent No. 5,795,725), Baig (American Heart Journal, 1998, 135: S216-S230), Kline et al. (Annals of

Emergency Medicine, Feb. 2000, 35: 168-180), and Zweig et al. (Clinical Chemistry, 1993, 39: 567-577), and further in view of Holvoet et al. (U.S. Patent No. 6,309,888). Applicants do not agree that claims 5-8, 13, and 14 are obvious over the cited references. However, to advance prosecution, and not in acquiescence to the rejection, Applicants have amended claim 1. For the reasons provided in the response to the prior obviousness rejection, Applicants assert that the claims 5-8, 13, and 14 that depend from claim 1 are nonobvious with respect to the cited references.

Holvoet et al., cited for disclosure of diagnosis of MI, does not make up for the deficiencies of Jackowski, Buechler et al., Baig, Kline et al., and Zweig et al. in that Holvoet et al. does not disclose differential diagnosis of MI, PE, and CHF. Claims 6 and 14 have been canceled without prejudice, rendering their rejection moot. Claims 5, 7, 8, and 13 are nonobvious under 35 USC § 103(a) for the same reasons claim 1, from which they depend, is nonobvious. In view of the foregoing, Applicants respectfully request that the rejection of claims 5, 7, 8, and 13 be reconsidered and withdrawn.

Rejection of claim 17 under 35 USC § 103(a)

Claim 17 has been rejected under 35 USC § 103(a) as allegedly obvious over Jackowski (U.S. Patent No. 5,710,008) in view of Buechler et al. (U.S. Patent No. 5,795,725), Baig (American Heart Journal, 1998, 135: S216-S230), Kline et al. (Annals of Emergency Medicine, Feb. 2000, 35: 168-180), and Zweig et al. (Clinical Chemistry, 1993, 39: 567-577), and further in view of Heeschman et al. (The Lancet, 1999, 354: 1757-1762). Applicants do not agree that claim 17 is obvious over the cited references. However, to advance prosecution, and not in acquiescence to the rejection, Applicants have amended claim 1 and have also amended claim 17. Claim 17 as amended recites a method according to claim 1, in which the amount of BNP assayed is compared to a predetermined threshold level. Applicant assert that claim 17 as amended is nonobvious with respect to the cited references.

Heeschan et al. cited for disclosure of comparing patient troponin T levels to a predetermined threshold, does not make up for the deficiencies of Jackowski, Buechler et al., Baig, Kline et al., and Zweig et al. in that Heeschan et al. does not disclose differential diagnosis of MI, PE, and CHF. Claims 17 is therefore nonobvious under 35 USC § 103(a) for the same reasons claim 1, from which it depends, is nonobvious. In view of the foregoing, Applicants respectfully request that the rejection of claim 17 be reconsidered and withdrawn.

Obviousness-Type Double Patenting

With regard to the Examiner's provisional rejection for obviousness-type double patenting, Applicants request that provisional obviousness-type double patenting rejections be held in abeyance until the claims as amended herein have been examined and all other rejections have been overcome.

Applicants further note that no terminal disclaimer is procedurally required in a case where the provisional rejection involves two pending applications and where the rejection is the sole remaining issue in the case. See MPEP § 804 (I)(B) (The "provisional" double patenting rejection should continue to be made by the examiner in each application as long as there are conflicting claims in more than one application unless that "provisional" double patenting rejection is the only rejection remaining in at least one of the applications.).

In the event that other rejections of the present claims are successfully overcome by the current communication, withdrawal of the provisional rejections based on pending applications would be appropriate.

CONCLUSION

Applicant respectfully submits that all rejections and objections have been obviated and that the pending claims are in condition for allowance. An early notice to that effect is earnestly solicited. Should any matters remain outstanding, the Examiner is encouraged to contact the undersigned at the telephone number listed below so that they may be resolved without the need for an additional action.

A response to the Office Action was first due April 4, 2008; and the first extension for response with one extension of time is August 4, 2008. Applicants, therefore petition for a one-month extension of time and provided with this electronic filing the associated fee. The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16 1.17, or credit any overpayment, to Deposit Account No. 23-2415.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (858) 350-2392.

Respectfully submitted,

WILSON SONSINI GOODRICH & ROSATI
Professional Corporation

Date: August 4, 2008


Elizabeth A. Orr
Registration No. 45,937

650 Page Mill Road
Palo Alto, CA 94304
(650) 493-9300
Customer No. 021971